REMARKS

Claims 1-35 are pending. Claims 30-35 are withdrawn.

Objections to the Claims

The Examiner objects to claims 1 and 16 for reciting both polyethyleneimine and polyethylenimine. Applicants submit that the claims were amended in the Response dated October 5, 2007. In a telephone conversation with the Examiner on July 14, 2008, the Examiner indicated that the amendments in the paper of October 5, 2007 were not entered, despite Applicants' filing of an RCE on December 5, 2007 requesting such entry. By the October 5, 2007 Amendment, which Applicants understand to have been entered per a conversation with Examiner Popa on August 12, 2008, the term "polyethylenimine" is now spelled consistently throughout the application. Applicants thank Examiner Popa for her time and consideration of this Application.

Rejections under 35 U.S.C. §103

The Examiner rejects claims 1, 2, 5-19 and 21-29 under 35 USC § 103(a) as being unpatentable over Davis WO '885 in view of Gosselin (2001), Cheng US '808 and Wachter (1986).

The Examiner states that Davis teaches a biodegradeable, linear cyclodextrin block copolymer and a method of synthesizing the block copolymer by modifying ß-cyclodexterin with a linear polycationinic co-monomer such as spermine (i.e. a transfection agent) to form a block copolymer wherein cyclodextrin is attached to spermine and not to another cyclodextrin moiety. The Examiner states that this co-polymer is capable of complexing with nucleic acids and is suitable for nucleic acid delivery to a cell.

The Examiner states that Davis '885 does not teach a cyclodextrin block copolymer wherein the co-monomer is low molecular weight PEI. However the Examiner states that Gosselin discloses that high molecular weight PEI is toxic to the cells and teach replacing it with high molecular weight biodegradable conjugates composed of cross-linked 800 Da PEI. The Examiner states that it would

have been obvious to modify the copolymer of Davis by replacing their transfection agent with the transfection agent of Gosselin with a reasonable expectation of success. The Examiner states that the motivation to do so is provided by Gosselin, who teaches that PEI is a very efficient transfection agent which also offers advantages over the other transfection agents. Applicants respectfully traverse.

Applicants submit that one of skill would not combine Gosselin with Davis because Gosselin teaches away from the present invention. Specifically, the Examiner states that one of skill would look to Gosselin because Gosselin discloses that the toxicity of high molecular weight PEI is reduced by cross-linking. Gosselin teaches away from using uncrosslinked low molecular weight PEI, and also teaches away from using even lightly cross-linked PEI. (Gosselin, 991, col. 1, lines 61-62, 800 Da PEI was the least effective transfection agent, and 1,800 Da PEI is stated to convey negligible gene expression). The ratio of cross linking in Gosselin is *significantly above* that disclosed in the present invention; claim 1 recites that the PEI used is linear, ie. not crosslinked. Specifically, Gosselin describes the cross linking ratio of primary amine:imidoester reactive group of 2:1 as being "relatively ineffective," and lauded the cross-linking ratio of 1:1. (Gosselin 991, col. 2, lines 2-8). Either ratio is significantly greater than that disclosed in the present invention. Thus, one of skill in the art would not have any expectation that a copolymer of cyclodextrin and one or two low molecular weight linear PEIs in the form of a linear, alternating co-polymer and not to any other cyclodextrin molecule would be a successful transfection agent. Accordingly, the Examiner fails to establish *prima facie* obviousness of the invention over Gosselin and Davis and the instant rejection should be withdrawn.

Furthermore, the present invention shows unexpected efficacy in in vivo experiments. Compared with Davis, gene delivery efficiency of PEI is superior to that of spermine. For example, Applicants show that the polymer of the invention is capable of in vivo delivery. (See Specification page 12, lines 11-21). In contrast, there is no published data on in vivo gene delivery by spermine.

Over Davis, Gosselin, in view of Cheng et al.

Claims 1, 2, 5-19, and 21-29 are rejected under 35 USC § 103(a) as being unpatentable over Davis '885 and Gosselin in view of Cheng et al. US 2004/0077595 (hereinafter Cheng '595). This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner states that Davis and Gosselin do not teach cross-linking cyclodextrin and PEI via an ester bond. The Examiner states that Cheng teaches that linking cyclodextrin to PEI via an ester bond.

It is very apparent that Cheng '595 relates to branched polymers. This is evident merely from examination of formulae (I), (II) and (III) of the reference. Thus, Cheng '595 expressly teaches away from the present invention, which due to the features described in claim 1 is a linear polymer. Furthermore, formula (III) of Cheng '595 shows a central CyD molecule having four "linker" groups; this embodiment includes linkages in excess of two to the CyD molecule, as recited in the present claims. Thus one of skill would not combine Davis with either Gosselin or Cheng with any expectation of success in making the presently claimed invention. Applicants submit that the combination of Davis, Gosselin, and Cheng fail to establish *prima facie* obviousness of claims 1, 2, 5, and 21-29 and request that the Examiner withdraw the instant rejection.

Over Davis, Gosselin, in view of Cheng and Wachter

The Examiner cites Wachter for the proposition that the art teaches that 1,1'-carbonyldiimidazole can be successfully used to link hydroxyl and amine groups, therefore it would have been obvious to use 1,1'-carbonyldiimidazole to achieve the result of coupling cyclodextrin to PEI. However claims 9, 10, 18, and 19 incorporate claims 1 and 16, wherein each cyclodextrin moiety is attached to one or two PEI moieties and not to any other cyclodextrin moiety and that the PEI is less than 10 kDa molecular weight. Wachter does not address the failure of the Davis and Gosselin references to suggest these features of the invention. Furthermore, Wachter describes linking of carbonyl diimidazole nucleic acid to biotin through hexamethylene diamine. There is

no suggestion whatsoever by Wachter that the carbonyldiimidazole reagent is suitable for forming a linear co-polymer of cyclodextrin with a polyethylenimine, i.e., that two large polymeric molecules could be effectively joined to form a linear, alternating co-polymer. Thus the combined references do not establish *prima facie* obviousness of the claimed invention. Consequently, Applicants request that the Examiner withdraw the rejection.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Dr. Mark Nuell, Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

By 

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